AMENDMENTS TO THE CLAIMS

Claim 1 (Currently amended) A method ~~for interfering with the expression of hyphal-specific genes in a fungus resulting in the inhibition of cell growth of said fungus~~ comprising the step of:

interfering with the transcription of ~~said~~ hyphal-specific genes in *C. albicans* mediated by *cis* acting sequences, wherein cell growth of said *C. albicans* is inhibited.

Claim 2 (Cancelled)

Claim 3 (Cancelled)

Claim 4 (Original) The method of claim 1, wherein said *cis* acting sequences comprise *cis*-regulatory elements.

Claim 5 (Original) The method of claim 4, wherein said *cis*-regulatory elements comprise UAS.

Claim 6 (Original) The method of claim 4, wherein said *cis*-regulatory elements comprise URS.

Claim 7 (Original) The method of claim 4, wherein said interfering step comprises interfering with DNA BP that bind to said *cis*-regulatory elements.

Claims 8-10 (Cancelled)

Claim 11 (Original) The method of claim 7, wherein said interfering with DNA BP comprises manipulating the binding of said DNA BP to said *cis* regulatory elements.

Claims 12-18 (Cancelled)

Claim 19 (Amended) The method of claim 1, wherein said hyphal-specific gene comprises the HWP1 gene.

Claim 20 (Original) The method of claim 19, wherein said HWP1 gene contains cis acting sequences within its promoter region.

Claim 21 (Original) The method of claim 20, wherein said HWP1 promoter region comprises the following isolated DNA sequence [SEQ. ID. NO:1]:

GGATCTTTCTTTTTCATTTCCCTTAAAACCGATCAAGAAAGAAAGTGGAAATAAA
GCTATGATAAATGTTGATTTTGTGTAATTCAATCAACTAAGCACGTTTGACAGTT
AAAAAGTACGTTGTTGTTGTCCTCGTCTCGTCTAATTTCTGTTGACGAGGATTAAT
AACAAGAAATACAGGAAACCCTCCAAAAAAAAAAATTTTGGACCTTACACGCACA
TAAATTGCGGATAAACTTGCCATAATAAAAACTCTTTGAAACATACGATATGTTA
TTCTTTTCATAACTGGAATATTTTTGCTTTTTTTTAACATTATGAACAATTGAAAA
AAAAAGGAAATGAAAAGGTAAGAGTTGCCTAACCATTGAAAATAATAGGCTAAG
GTTTTTCCTGATGCGTTTAACTAAAAAGGAAATAACAAAAGTTATTAGCGATAAC
CTGCGTAAGGTGTCAACAAAATATATTTTGCACGTTAGCTCTATAGAAAATATAC
AAACTAAATCCTTAAGGAATTTCCTCTATATATAATAGGAAATCCCTCTCACAGT
GAACTGAATTATCCATCTGAATTATCAGTCCACTAATTCCATCAATAAAATAGAT
TAGTGTATTGTTCTCTTCAGTACAATTACTACCATTATGCAATGCTAGCTTATTGT
TCATAATTAGCCATGTTGCACACCCTAATTCGAACATTAACTGTATCCATATTTTT
CTTGTCCTTCTTTGTTTTTTTCTAACAAAAATGTTCCAGAATTTTTTAAAAAATATT
TGAAAAAACACATAACACTTTGAGTATGATAATATCAACTATTGACTTGTTTTGA
AAGTAAAGAATCAAATTTTTTTCTAACTCGACTAATGCACTTTACATCAACTGGA
TGTTATTTGCATCTACTACTATAAGCTCAAACAAATTATCTTTCAAAAATGTTATA
ATTAACAAGTCATCTATAATTCTTTGGATCCAAAAACAAGGAATTCGGAAATTCT
GACGATAAATGTCGACTCACAATTCATTGTAAAAAGGGAGAGTTTTGGTAGGCTC
ATAATCGCTTATAATGTACCTCTAAAGTAATCTAAAACAAACACAACCTTTCTAA
AACCTATAATAATAACCCTAATGGCTCACAACCGGGATAATGTTAGTTAGCCCAG
CTGTTTTTTTTTTGCCTTATTTTTATGACTACATTTTGTTTCACTTTTTGTTGCGACT
TTAATACCGTTTTTGCAACTTCTCTTTGTATCACCTGTATCCGCCTTTTTTAACATA
GCAACTCTTGTAAAGTCCCTTTCTTTTCCCACTATTTTATCATTCTTGAAATATGT
AATCAGAATAGTTTTTCAAAAACTATAAATAACGGTCAAAATAACCGGCTATTTT
CAATTTCCATTCAACTTGTTTTCTCAACAATATCAAACACAACAGGAATCTCCTAT
AGTCACTCGCTTTTAGTTTCGTCAATATG;

including any insertions, deletions, mutations, or modifications.

Claims 22-26 (Cancelled)

Claim 27 (Amended) The method of claim 1, wherein said hyphal-specific genes ~~comprise genes~~ are responsible for controlling dimorphism.

Claim 28 (Original) The method of claim 4, wherein said *cis*-regulatory elements comprise a NIT2 binding site.

Claim 29 (Original) The method of claim 7, wherein said DNA BP is encoded by a nucleotide sequence for the DNA binding domain that is homologous to a nucleotide sequence encoding the DNA binding domain of NIT2 binding proteins.

Claim 30 (Original) The method of claim 29, wherein the DNA BP is selected from the group consisting of GAT99, GAT-1, or GATA-like binding proteins.

Claim 31 (Original) The method of claim 29, wherein said NIT2 DNA binding domain comprises the protein sequence [SEQ. ID. NO: 2]:
CTNCFTQTTPLWRRNPDGQPLCNACGLFLKLHGVVRPLSLKTDVIKKRNR.

Claim 32 (Original) The method of claim 29, wherein the DNA binding domain of said DNA BP comprises the protein sequence [SEQ. ID. NO: 3]:
CTNCGTKTTPLWRRNPQGQPLCNACGLFLKLHGVVRPLSLKTDVIKKRQR.

Claims 33-43 (Cancelled)

REMARKS

Applicant thanks Examiner Zara for the courtesies extended during the telephonic interviews held with the undersigned on 7 February 2003 and on 25 September 2003. As reflected in the Interview Summary dated 7 February 2003, the non-response, mailed on 13 January 2003, addressing the election made by the Applicant on 25 July 2002 to the restriction requirement has been vacated. Accordingly, the claims within the elected Group III will be examined on the merits.

The Examiner acknowledges Applicant's election, with traverse, of Group III, stating that the "traversal is on the ground(s) that the inventions of the different groups are not *patentably distinguishable* inventions..." (emphasis added). Paper No. 10 at page 2. This statement is not correct. Applicant never stated that the inventions are not patentably distinguishable, but rather that "Groups I-IX are related and...are capable of use together." and that the Examiner had "failed to establish that the alleged inventions are distinct from each other." Paper No. 5 at pages 3-4

Applicant acknowledges that the drawings filed on 29 November 2000 were accepted.

Claims 1-43 are pending. Claims 2-3, 8-10, 12-18, 22-26 and 35-43 have been cancelled. Applicant reserve the right to file one or more divisional applications directed to the subject matter of the non-elected claims.

The amendments to the pending claims are made to more clearly define the inventions. It is submitted that the amendments introduce no new matter and entry of the same is respectfully requested. By these amendments, the Applicant does not acquiesce to the propriety of any of the Examiner's rejections and do not disclaim any subject matter to which the Applicant is entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q.2d 1865 (U.S. 1997).

I. REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

A. Claims 1-7, 11, 19-21 and 27-32 are rejected under 35 U.S.C. § 112, first paragraph

The Examiner alleges that claims 1-7, 11, 19-21, and 27-32 should be rejected under 35 U.S.C. § 112, first paragraph as "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Paper No. 10 at page 4. Applicant respectfully traverses.

In the present rejection, it appears that the Examiner is confusing the written description requirements for claims as described in *Regents of the Univ. of California v. Eli Lilly & Co.*, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997) with the method claims of the present invention. In *Lilly*, the Federal Circuit found a claim directed to human insulin cDNA invalid for failing to meet the written description requirement. *Id.* at 1400. The claims at issue were directed to vertebrate, mammalian, and human insulin cDNA. *Id.* at 1401. The specification, however, disclosed rat insulin cDNA and "provided only a general method for obtaining the human cDNA . . . along with the amino acid sequences of human insulin A and B chains." *Id.* at 1405.

Similar to the Examiner's wording of the rejection in the present application, the Federal Circuit stated that the specification "does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others." *Id.* at 1406. The Federal Circuit further explained that "a description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* (emphasis added). *See also, Fiers v. Revel*, 25 U.S.P.Q.2d 1601, 1606 (Fed. Cir. 1993) ("An adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself").

The claimed invention, however, is not directed to a genus of a gene (*Lilly)*, or as the Examiner believes, to a genus of hyphal specific genes, or cis acting sequences comprising cis regulatory elements, including UAS and UAR elements, or DNA binding proteins that bind to the claimed cis regulatory elements, or any insertion, deletion, mutation or

modification of SEQ ID NO:1. In distinct comparison, the claimed invention is directed to a method for interfering with the transcription of hyphal specific genes in *C. albicans* mediated by cis acting sequences. The Examiner's use of the *Lilly* rationale in the present case is inapposite and the present rejection should be withdrawn for this reason alone.

Nonetheless, and not in acquiesence to the Examiner's improper position above, Applicant wishes to point out that the hyphal specific genes, cis acting sequences and DNA binding proteins, as those terms are used in the claims, are fully described thoughout the specification, in satisfaction of 35 U.S.C. § 112, first paragraph.

Specifically, the Examiner alleges that the "specification and claims do not describe the elements that are essential to the broad genus comprising hyphal-specific genes." Paper No. 10 at page 4. Applicant disagrees. Indeed, Applicant submits that hyphal specific genes are adequately described throughout the specification. For example, on page 21, lines 32-33, the specification discloses several references, which are properly incorporated by reference, that relate to and describe other hyphal-specific genes. Further, on page 22, lines 11-12, the specification states that other "hypha-specific genes include an aspartyl proteinase (SAP6) and proteins predicted to be localized to the cell wall (ALS3 and HYR)." Further, on page 72, lines 1-5, the specification discloses the hyphal specific genes HYR1, ECE1, ALS3, CHS2 and SAP6.

Next, the Examiner alleges that the "specification and claims do not describe the elements that are essential to the broad genus comprising...cis acting sequences comprising cis regulatory elements, including UAS and UAR elements." *Id.* Applicant disagrees. Examples of cis acting regulatory elements are adequately described throughout the specification. Both Figure 4 and its description found on page 8, lines 21-29, disclose the cis regulatory elements comprising NIT2, PHO4, HSF1 and MATA1.

Further, the Examiner alleges that the "specification and claims do not describe the elements that are essential to the broad genus comprising...DNA binding proteins that bind to the claimed cis regulatory elements." *Id.* Applicant disagrees. Examples of DNA binding proteins are adequately described throughout the specification. For example, page 25, lines 25- 32, describe the DNA binding proteins of the GATA family, which may bind to the NIT2 cis regulatory element. Further, page 26, lines 8-24 of the specification, describes the TUP1 DNA binding repressor protein, which may repress the expression of hypha specific genes.

In addition, the Examiner alleges that the "specification and claims do not describe the broad genus comprising any insertions, deletions, mutations or modifications of the hyphal specific sequence of SEQ ID NO:1." Paper No. 10 at page 4. Applicant disagrees.

Further, the Examiner alleges that "the specification does not place any limit of the number of nucleic acid or amino acid substitutions, deletions, insertions and or modifications of SEQ ID NO:1." *Id.* Applicant disagrees. Applicant asserts that one skilled in the art would know and it would be a matter of routine experimentation to determine which insertions, deletions, modifications or mutations could be made to SEQ ID NO:1, in the context of the present invention. All such insertions, deletions, mutations or modifications of SEQ ID NO:1, need not be specifically described

Finally, the Examiner alleges that "since the disclosure fails to describe the common attributes or characteristics concisely identifying members of the proposed genus...the description provided...is insufficient." *Id* at page 5. Applicant disagrees. As described above, Applicant submits that the specification discloses the members of the proposed genus, as to satisfy § 112 first paragraph. Moreover, as discussed above, the entire premise of the present rejection is faulty in that the Examiner's arguments based on the *Lilly* rationale for compound claims is inapposite to the presently claimed methods. Accordingly, Applicant asserts that the present application is in full compliance with the written description requirement and respectfully requests reconsideration and withdrawal of the present rejection.

B. Claims 1-7, 11, 19-21 and 27-32 are rejected under 35 U.S.C. § 112, first paragraph

The Examiner alleges that "claims 1-7, 11, 19-21, 27-32 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabled for measuring expression patterns of HWP1 mRNA and HWP1 protein...does not reasonably provide enablement for the ability to interfere with the expression of any and/or all hyphal specific genes." *Id.* Applicant respectfully traverses.

Specifically, the Examiner alleges that the "Applicants have not provided guidance in the specification toward a method of interfering with the expression of any and/or all hyphal specific genes." *Id.* at page 7. Further, the Examiner alleges that "one skilled in the art would not accept on its face the examples given in the specification of purported cis acting sequences identified by sequence alignment as being correlative or representative of the ability to interfere with...hyphal specific genes in a fungus." *Id.* at pages 7-8.

Applicant submits the specification adequately enables a person skilled in the art to make and use the claimed invention. First, as described above, the specification adequately describes *C. albicans* hyphal specific genes, cis regulatory sequences present within the

promoter region of *C. albicans* hyphal specific genes, and DNA binding proteins that are capable of binding to the cis regulatory elements.

Further, the specification provides adequate disclosure to enable one skilled in the art to make and use the claimed invention. Applicant refers the Examiner to the working examples of the specification beginning on page 50: example 1, starting on page 50, provides a detailed description for determining the structural features of a gene product; example 2, beginning on page 54, provides a detailed description for determining the transcriptional regulation of a gene product, a methodology for identifying the cis acting sequences present within the gene product and a description for identifying the DNA binding proteins that may interact with the cis acting sequences within the gene product; example 3, beginning on page 57, provides a detailed description for examining the regulation of the promoter region of a gene by generating a fusion reporter construct; example 4, beginning on page 62, provides a detailed description for identifying UAS and URS elements that regulate gene expression; example 5, starting on page 65, provides a method for identifying and characterizing DNA binding proteins that regulate a gene promoter; and example 6, beginning on page 71, provides a detailed description of identifying global regulatory networks by isolating genes that are co-regulated with a gene by using mini-array technology. Applicant asserts one skilled in the art would understand that the methods provided may be used for any hyphal specific gene in the context of the present invention.

Next, the Examiner cites to the references of Csank et al., Braun et al., and DeBernardis et al., and concludes that the "field of transcriptional regulation of hyphal specific genes is still in its infancy and hence highly unpredictable at the current time." *Id.* at page 7. Applicant asserts that the Examiner's rejection is improper and without basis in law or fact. As discussed above, Applicant fully complies with the requirements of 35 U.S.C. § 112, first paragraph. The Examiner must address the subject matter disclosed and claimed in the present invention and not what is allegedly suggested in the cited studies. In addition, the references cited by the Examiner do not specifically relate to the claimed invention. The Examiner's cited references are related to the interaction between various signal cascades and the regulation of transcription factors. The claimed invention relates to methods for interfering with the transcription of hyphal specific genes mediated by cis acting sequences.

Finally, the Examiner alleges that the "quantity of experimentation required to practice the invention as claimed would require *de novo* determination of the cis acting sequences mediating any and/or all hyphal specific genes...would require undue experimentation." *Id.* at pages 8-9. Applicant disagrees. To determine what constitutes

undue experimentation in a given case, a standard of reasonableness, in light of the nature of the invention and the state of the art at the time the patent application was filed should be applied *See In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986). A list of factors to be considered when determining whether a specification requires undue experimentation include: "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *See Wands*, 858 F.2d at 737.

As set forth in detail above, Applicant submits that there is adequate direction and guidance in the specification, that the specification provides a number of working examples, that there was a high level of skill in the art at the time the application was filed, and that all of the methods needed to practice the invention are well known. Further, Applicant submits that the specification does not have to exemplify every aspect of the claim to enable the full scope of the claimed invention, and that the specification, set forth in detail above, does contain the requisite amount of detail to enable those of ordinary skill in the art to make and use the invention as claimed. *See In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991). Therefore, Applicant asserts that it would not require undue experimentation to one skilled in the art in view of the present specification, to identify, for example, cis regulatory sequences located within hyphal specific genes. Accordingly, Applicant submits that the specification is in full compliance with the requirements under 35 U.S.C. § 112, first paragraph and respectfully requests reconsideration and withdrawal of the present rejection.

II. CONCLUSION

Applicant has properly and fully addressed each of the Examiner's grounds for rejection. Applicant submits that the present application is now in condition for allowance. If the Examiner has any questions or believes further discussion will aid examination and advance prosecution of the application, a telephone call to the undersigned is invited. Also, filed concurrently is a Request for Examiner Interview. Applicant respectfully requests a personal interview in the presence of Examiner Zara along with her Supervisory Patent Examiner.

If there are any additional fees due in connection with the filing of this amendment, please charge the fees to undersigned's Deposit Account No. 50-1067. If any extensions or fees are not accounted for, such extension is requested and the associated fee should be charged to our deposit account.

Respectfully submitted,

2 October 2003

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